

**REMARKS**

Claims 1-8 and 32 are pending. Claims 9-31 have been previously withdrawn. Claim 1 has been amended to address terms stated by the Examiner to be indefinite. The subject matter of claim 32 has been additionally incorporated into claim 1(b). Claim 32 has been cancelled.

Response under 35 U.S.C. § 102(e)

The Examiner states that the Muir et al. reference, which was filed in November 1998, describes the claimed invention. In support of this statement, the Examiner has cited col 23, lines 30 and 49; col 24, lines 10, 26, 27, 28, and 33-34, and col 32, lines 23, 24, 28 and 30.

Claim 1 upon which claims 2-8 depend requires is a method for purifying a ligand-binding molecule from a mixture that requires (a) forming a carrier-ligand conjugate by reacting a C-terminal thioester on a carrier with a nucleophilic group on a ligand or a C-terminal thioester on a ligand with a nucleophilic group on a carrier, wherein cleaving a carrier-intein fusion protein or a ligand-intein fusion protein generates the C-terminal thioester; (b) binding the carrier-ligand conjugate to a matrix and contacting the carrier-ligand conjugate with a mixture containing the ligand-binding molecule to selectively bind the ligand-binding molecule to the carrier-ligand conjugate; and

(c) eluting the ligand-binding molecule from the ligand so as to obtain the purified ligand-binding molecule.

The claimed invention requires in (a) that the carrier and ligand be covalently linked to each other before the carrier-ligand conjugate becomes bound to the matrix and the ligand-binding molecule. In (b), the ligand-binding domain is selectively bound to the ligand after the carrier-ligand conjugate is bound to the matrix. This feature is summarized in Figure 19. In Figure 19, the carrier is linked to the ligand by a covalent bond (solid line) to form the carrier-ligand conjugate. However, the ligand is shown to be non-covalently associated with the ligand-binding domain at one end of the conjugate and the carrier is shown to be non-covalently associated with the matrix at the other end of the conjugate. The characteristic of non-covalent binding of the carrier to the matrix and the ligand to the ligand-binding domain is also consistent with the definitions of carrier and ligand on pages 17 and 18. In (c) the ligand-binding molecule is eluted from the ligand.

This method is effective because the ligand-binding molecule can be eluted from the ligand under conditions where the carrier remains bound to the matrix. This yields a purified ligand-binding molecule.

Advantages of the method include the ability to use a large molecule as a carrier, which is exploited as shown in the examples. For example, Example VI describes the use of the claimed invention

Rejection under 35 USC 102(e)

The Examiner has rejected the claims as anticipated by Muir.  
( '594 reference)

The Muir reference requires that the carrier be a small synthetic peptide that is covalently bound to a matrix (chip) (Column 31, line 24 of the '594 reference). Once bound, the peptide is covalently linked to a ligand using intein mediated ligation developed by Applicants previously (Figure 2A of the '594 reference), the technology being sold by New England Biolabs (assignee) and referred to by Muir (column 23 line 34).

There is no suggestion in Muir that a ligand-carrier conjugate be formed before attachment to the matrix as now required in the claimed invention. There is no suggestion in Muir et al that the peptide be associated with the chip by any means other than by covalent linkage nor is there any suggestion of the advantages or challenges of pursuing the claimed invention. The Muir et al reference does not describe how the ligand-binding molecule might be eluted from the protein array. In particular, it does not teach or suggest how the ligand-binding molecule might be eluted from the protein array under circumstances where an affinity bound carrier might remain attached.

In summary, the '594 reference does not describe or suggest the claimed purification method. The Examiner is

Xu et al.

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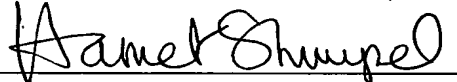
therefore respectfully requested to reverse the rejection  
under 35 USC 112(e).

**CONCLUSION**

For the reasons set forth above, Applicants respectfully request that the rejections set forth in the Final Official Action of November 21, 2005 be withdrawn and submit that this case is in condition for immediate allowance. Early and favorable consideration leading to prompt issuance of this Application is earnestly solicited. Applicants petition for an extension of three months and enclose a check for \$760 covering the extension fees and the fee for the attached notice of appeal. We authorize that any additional fees that may be due be charged to deposit account number 14-0740.

Respectfully submitted,

NEW ENGLAND BIOLABS, INC.



Harriet M. Strimpel, D.Phil.

(Reg. No.: 37,008)

Attorney for Applicant

240 Country Road

Ipswich, Massachusetts 01938

(978) 380-7373

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Customer No.: 28986